

The WNT receptor FZD7 is required for maintenance of the pluripotent state in human embryonic stem cells.

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Public Summary:

WNT signaling is involved in maintaining stem cells in an undifferentiated state; however, it is often unclear which WNTs and WNT receptors are mediating these activities. Here we examined the role of the WNT receptor FZD7 in maintaining human embryonic stem cells (hESCs) in an undifferentiated and pluripotent state. FZD7 expression is significantly elevated in undifferentiated cells relative to differentiated cell populations, and interfering with its expression or function, either by short hairpin RNA-mediated knockdown or with a fragment antigen binding (Fab) molecule directed against FZD7, disrupts the pluripotent state of hESCs. The FZD7-specific Fab blocks signaling by Wnt3a protein by down-regulating FZD7 protein levels, suggesting that FZD7 transduces Wnt signals to activate Wnt/ β -catenin signaling. These results demonstrate that FZD7 encodes a regulator of the pluripotent state and that hESCs require endogenous WNT/ β -catenin signaling through FZD7 to maintain an undifferentiated phenotype.

Scientific Abstract:

WNT signaling is involved in maintaining stem cells in an undifferentiated state; however, it is often unclear which WNTs and WNT receptors are mediating these activities. Here we examined the role of the WNT receptor FZD7 in maintaining human embryonic stem cells (hESCs) in an undifferentiated and pluripotent state. FZD7 expression is significantly elevated in undifferentiated cells relative to differentiated cell populations, and interfering with its expression or function, either by short hairpin RNA-mediated knockdown or with a fragment antigen binding (Fab) molecule directed against FZD7, disrupts the pluripotent state of hESCs. The FZD7-specific Fab blocks signaling by Wnt3a protein by down-regulating FZD7 protein levels, suggesting that FZD7 transduces Wnt signals to activate Wnt/ β -catenin signaling. These results demonstrate that FZD7 encodes a regulator of the pluripotent state and that hESCs require endogenous WNT/ β -catenin signaling through FZD7 to maintain an undifferentiated phenotype.

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